


# 27 – Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD



**INFECTIONIOUS DISEASE BOARD REVIEW**  
AUGUST 17-21, 2024

## Ticks, Mites, Lice, and The Diseases They Transmit

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7/1/2024



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- Disclosures of Financial Relationships with Relevant Commercial Interests
  - Consultant: Gilead, Shionogi
  - Research Grant: Pfizer
  - Ownership Interest: Johnson & Johnson

Why the board exam loves these infections  
PLAY THE MATCH GAME

Condition	Pathogen
• Scrub typhus	• <i>Rickettsia conorii</i>
• Louse-borne relapsing fever	• <i>Rickettsia prowazekii</i>
• Tick-borne relapsing fever	• <i>Borrelia recurrentis</i>
• Boutonneuse (Mediterranean) fever	• <i>Borrelia hermsii</i>
• Louse-borne epidemic typhus	• <i>Borrelia turicatae</i>
• Endemic (murine) typhus	• <i>Rickettsia typhi</i>
	• <i>Orientia tsutsugamushi</i>

## Tick-borne Diseases of North America General Principles I

- Initial, early presentation non-specific:
  - “Flu-like illness” (e.g. fever, headache, myalgia)
- Diagnosis is clinical
  - Treatment is empiric—must start prior to return of diagnostic testing
- Characteristic rash/lesion +/- especially early
- Asymptomatic:symptomatic ratio is high

Ref: Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsioses, Ehrlichioses, and Anaplasmosis — United States. A Practical Guide for Health Care and Public Health Professionals, MMWR May 13, 2016 / 65(2);1–44

## Tick-borne Diseases of North America General Principles II

Seasonal but not always  
Geography informs etiology but often changes over time  
Lab tip-offs:

- Thrombocytopenia
- Leukocytosis or leukopenia
- Elevated LFTs

Doxycycline is preferred therapy for most  
(all ages including children, e.g., Lyme, RMSF, ehrlichiosis...)  
Prognosis is worse at age extremes < 10 and > 60 yrs  
Tick vectors

- Ticks cause 95% of vector borne disease in the US
- Co-infections in some patients

## The Major Tick-borne Diseases of North America

- Lyme disease (separate talk)
- Rocky Mountain spotted fever (RMSF)
- Ehrlichioses
- Anaplasmosis
- Relapsing fever (*Borrelia* spp.)
- Babesia spp.

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## Other Tick-borne Diseases of North America

- Tick paralysis
- Southern tick associated rash illness (STARI)
- Viruses:
  - Powassan (Deer Tick Virus Lineage II, flavivirus)
  - Colorado tick fever (coltivirus)
  - Heartland virus (phlebovirus)
  - Bourbon virus (thogotovirus)
- Spotted Fever Group Rickettsia (partial)
  - *R. parkeri*
  - Rickettsia 364D aka *R. philippii* (Pacific Coast tick fever)
- Coxiella burnetii
- Tularemia
  - (< 10% tickborne)
- Other Borrelia
  - *B. miyamotoi*
  - *B. mayonii*

## Ticks: arachnids, not insects

- Number of species
  - >900 species or subspecies world wide
  - 90 species in North America, handful cause most human infections
- Hematophagous arthropods
  - parasitize every class vertebrates  $\approx$  entire world
- Two major families
  - Ixodidae, >700 species (hard ticks, attach & engorge)
  - Argasidae, >190 species (soft ticks, bite multiply & briefly)
- Four basic life stages
  - egg  $\rightarrow$  larva  $\rightarrow$  nymph  $\rightarrow$  adult
- Vectors of human disease
  - #1 mosquitoes
  - #2 ticks

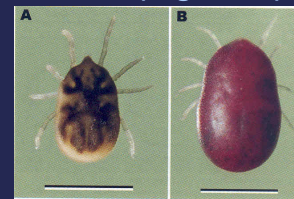
Parola, Raoult CID 2001; 32:897-928  
Guglielmo, Zootaxa 2010;2528:1-28  
Eisen, Ticks Tick Borne Dis 2022;12(6):102025

## Top Ticks in North America That Transmit Human Pathogens (Ixodidae)

#1 *Ixodes scapularis*  
#2 *Amblyomma americanum*  
#3 *Dermacentor variabilis*  
#4 *Ixodes pacificus* (Western black-legged tick)  
#5 *Dermacentor andersoni* (Rocky Mt wood tick)

Eisen, Ticks Tick Borne Dis 2022;12(6):102025

## *Ornithodoros Hermsi* nymphal Tick Soft tick (Argasidae)



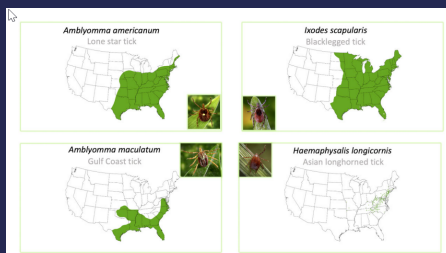
A: shows the nymph before its infective blood meal (from California)

B: shows it after feeding

These are soft ticks that feed briefly at multiple spots—DO NOT remain attached

Scale bars = 2 mm

## Expanding Range and Ticks New to the US



*I. scapularis*  
-Ticks that carry *B. burgdorferi* and bite humans mostly northern tick populations

*H. longicornis*  
May carry multiple pathogens, participation in transmitting to humans occurs but uncertain to what degree

Molaei, JID 2022;226(3):370-373

## Selected Tickborne Diseases in the US

Home	Data Summary	Cases by Year	Cases by Month	
<b>Tickborne Disease Surveillance Data Summary</b>				
Total Reported Cases by Tickborne Disease, 2019-2022				
Disease	2019	2020	2021	2022
Lyme disease	34,945	18,010	24,611	62,551
Anaplasmosis	5,655	3,639	6,744	5,633
Spotted fever rickettsioses	5,207	1,175	1,278	1,271
Ehrlichia chaffeensis ehrlichiosis	2,093	1,180	1,347	1,557
Babesiosis	2,418	1,827	1,915	
Tularemia	274	150	162	167
Undetermined ehrlichiosis/anaplasmosis	185	50	77	95
Powassan virus disease	43	21	24	47
Ehrlichia ewingii ehrlichiosis	43	21	19	25
<b>Total</b>	<b>50,863</b>	<b>26,073</b>	<b>36,177</b>	<b>71,346</b>

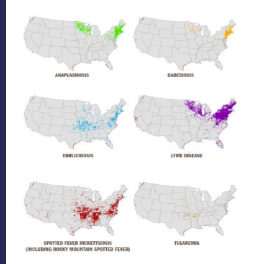
New 2022 CDC Surveillance Definition for Lyme disease

CDC, <https://www.cdc.gov/ticks/dtb-research/factsheets/tickborne-disease-surveillance-data-summary.html#:~:text=Current%202019%202022%202021%20and%202022%20new%20years,> (revised 6/22/24)

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### New regions for Common Tickborne Infections



**Range expanding for**

- Lyme disease
  - Upper Midwest
  - South along Appalachians
- Babesiosis
  - Expanding w/ Lyme disease range
- Ehrlichioses
  - *E. chaffeensis*, northward

CDC <https://www.cdc.gov/ticks/tickborneinfections/overview.html> Accessed 1/16/23

### Question #1: PREVIEW QUESTION

62M living in an exurb of Phoenix, Arizona presents in early September with a three day history of fever, myalgia, headache and rash.

He works as a lineman for a utility company. He lives with his family in an older adobe home with dogs. There is a faint maculopapular rash on extremities

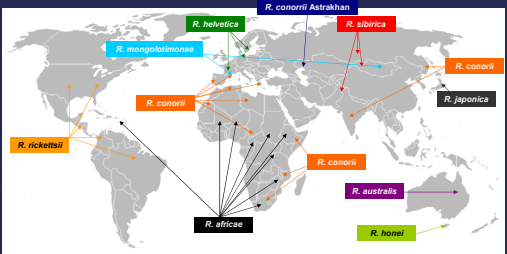
Which of the following is the most likely diagnosis?

- Human Monocytic Ehrlichiosis (HME)
- Human Granulocytic Anaplasmosis (HGA)
- Babesiosis
- Rocky Mountain Spotted Fever (RMSF)
- Tularemia

### Rickettsial species: two major groups (not a comprehensive rickettsial list)

Spotted Fever Group (SFG)	Typhus Group
<ul style="list-style-type: none"> <li>• RMSF (<i>R. rickettsii</i>)</li> <li>• <i>R. parkeri</i></li> <li>• <i>Rickettsia</i> sp. 364D</li> <li>• Rickettsialpox (<i>R. akari</i>)</li> <li>• <i>R. conorii</i></li> <li>• <i>R. africae</i></li> <li>• <i>R. japonica</i></li> <li>• <i>R. australis</i></li> <li>• ...many more</li> </ul>	<ul style="list-style-type: none"> <li>• Epidemic typhus                             <ul style="list-style-type: none"> <li>• <i>R. prowazekii</i></li> <li>• Body louse</li> <li>• Worldwide</li> </ul> </li> <li>• Murine/endemic typhus                             <ul style="list-style-type: none"> <li>• <i>R. typhi</i></li> <li>• Rat flea</li> <li>• Temperate–tropical, usually</li> </ul> </li> </ul>

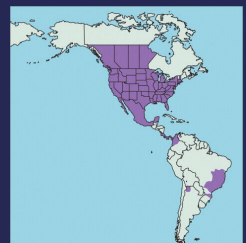
### Tick-borne Rickettsia World Wide: many species



> 24 species causing human disease. List continues to grow.

Parola, Clin Microbiol Rev 2013;26(4):657-702

### Approximate Geographic Distribution of *R. rickettsii* in the American Continents



See in all lower 48 states

Mexico

Parts of Canada

Central and South America

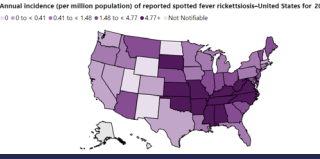
Ongoing epidemic in Northern Mexico (2015–present)

Alvaraz-Hernandez, Lancet ID 2017;17(6):e189-196  
Trinco-Garcia, EID 2018;24(9):1723-25

### CDC Changes:

--2010: RMSF to "spotted fever rickettsioses" 2010 due to lack of serologic specificity includes RMSF, *R. parkeri*, Pacific Coast tick fever, Rickettsialpox, and others

--2020: SFG criteria changes w/ IFA titer raise to  $\geq 1:128$  from 1:64 to raise specificity, elimination of IFA IgM ELISA



Source: CDC <https://www.cdc.gov/rocky-mountain-spotted-fever/data-research/facts-stats/index.html> (accessed 6/22/24)

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## SFR in the United States

### Incidence/Case Fatality 1920-2019



### Risk Factors for Fatal RMSF ('99-'07)

- Native Americans
- Age extremes: 5-9, 70+
- Use of chloramphenicol (not doxycycline)
- Delay in diagnosis:
  - Treatment after 5 days illness
- Immunosuppression

<https://www.cdc.gov/rocky-mountain-spotted-fever/data-research/facts-stats/index.html> (accessed 6/22/24)

Am J Trop Med Hyg 2012;86:713-9

## Rocky Mountain Spotted Fever Signs and Symptoms

Fever	99%
Headache	91%
Rash	88% (49% first 3 days)
Myalgia	83%
Nausea/vomiting	60%
Abdominal pain	52%
Conjunctivitis	30%
Stupor	26%
Edema	18%
Meningismus	18%
Coma	9%

Adapted from Helnick CG et al. *J Infect Dis* 150:480, 1984

## Rocky Mountain Spotted Fever

Early: rash absent or maculopapular  
Starts on extremities



Later rash: petechial



## Fulminant RMSF Gangrenous features (usually seen with multi-organ Failure)



## RMSF diagnosis and treatment

- Start treatment upon suspicion: DON'T WAIT
  - Mortality 4% if doxycycline w/i 5d of symptom onset; 35% if > 5d.
- Labs: leukocytosis, thrombocytopenia, transaminitis
- Dx:
  - Preferred:
    - Skin bxp immunohistochemistry (DFA): timely diagnosis, ~70% sensitive.
    - PCR: *R. rickettsii*-specific
      - Skin bxp or swab (not routinely available, contact local health department → CDC)

Jay R. *J Vector Borne Dis* 2020;57(2):114-120

## OUTCOME: RMSF ACCORDING TO THE DAY DOXYCYCLINE STARTED

	<u>% mortality</u>
Day 1-5	0
Day 6	33
Day 7-9	27-50

Most lethal of Rickettsial infections: "Black measles"

In US mortality with treatment ~2-5% (higher with delays)

*Clin Infect Dis* 2015; 60:1659-66

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### RMSF diagnosis and treatment

- Other diagnostics
- Culture: cell culture-based (BSL3 agent)
- Serology: obtain acute/convalescent samples
  - Not usually of timely clinical value.
  - IFA: gold standard; cross reacts w/ other SFG species.
    - May be helpful in confusing cases.
    - IgG is best to confirm
    - IgM with low specificity
- DON'T USE AS FEVER SCREENING TEST
- False positives (especially IgM) common
  - Georgia blood donor study 11.1% IgG > 1:64, but only 28% fit case definition for SFG (Straily A. JID 2020;221:1371)
  - Single IgG titer insufficient for reliable diagnosis
- Background seroprevalence up to 20% in some regions, e.g., Carolinas
  - Asx infection likely common
- Both RMSF IgM & IGG can persist
  - May mislead diagnosis, cause necessary treatment


### Question #2: PREVIEW QUESTION

31M from Tidewater region of Virginia presents in June with three days of fever and rash.

Exam: unremarkable but T39.2°C, discrete black eschar on leg, scattered maculopapular rash elsewhere

Which of the following is the most likely etiologic agent?

- A. *Rickettsia rickettsii*
- B. *Ehrlichia chaffeensis*
- C. *Rickettsia parkeri*
- D. *Anaplasma phagocytophilum*
- E. *Rickettsia akari*



### “American Boutonniuse Fever”

#### *Rickettsia parkeri*

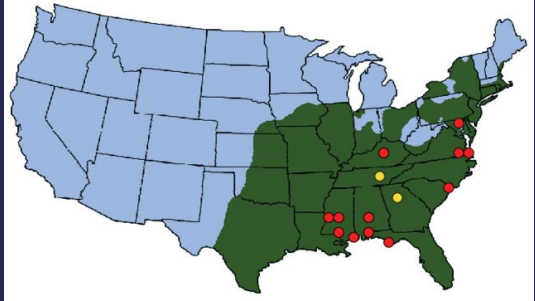
- Transmission: Lone Star or Gulf Coast ticks (*A. maculatum*)
  - Southeastern US, Gulf Coast
- AKA “Maculatum fever”
- Also seen in Central and South America including Argentina, Uruguay, parts of Brazil
- Symptoms 2-10d post-bite
  - Headache, myalgia
  - Skin
    - Faint salmon-colored rash
    - Single or multiple eschars
- Diagnosis
  - Spotted fever group serology,
  - Immunohistochemistry
  - PCR or culture from skin bxp or swab of eschar

MMWR Morb Mortal Wkly Rep 2016; 65(28): 718-9  
Kalinich, Infection 2018;46(4):555-563  
Scott, Trends in Micro 2022;28(5):511-512

### Examples of *R. parkeri*-associated rashes



Source: CDC



Green: Lone star tick range; Yellow: *A. maculatum* tick found; Red dots: *R. parkeri*

Note: Overlap of Lone star and Gulf coast tick range (Cohen SB. Emerg Infect Dis 2009; 15(9))

### Pacific Coast Tick Fever



*Rickettsia philippii* (*Rickettsia* 364D)  
Described in 2008

Transmitted by Pacific Coast tick (*Dermacentor occidentalis*)

Northern Baja → Southern Oregon, Most cases

Common symptoms:  
Eschar  
Fever  
Headache  
Usually mild infection

Usually single eschar

*Dermacentor occidentalis*

Pladgett K  
PLOS Neg Trop Dis 2016

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## Question #3

22M upstate NY July c/o HA and fever x 3d now confused. No known tick bite but an outdoorsman. Exam without meningism or rash. Labs normal.

Admitted, doxycycline, CTX, vancomycin started. Head CT: normal

LP: WBC 130 60%P, 40%L, glucose: nl, protein 65 mg/dL (elevated).

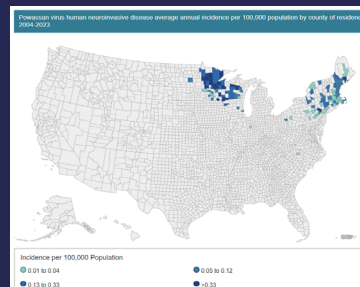
Which of the following is the most likely etiologic agent?

- A. Anaplasma phagocytophilum
- B. Ehrlichia chaffeensis
- C. Heartland virus
- D. Powassan virus
- E. Borrelia miyamotoi

## POW:

>Report cases mostly neuroinvasive  
>Tick-borne flavivirus infection

- Mostly present in Spring-Summer
  - But can be year round
  - Related to nymphal *Ixodes scapularis*
- All ages, median 62 years, 72% male
- Clinical Syndromes
  - Neuroinvasive (90%)
    - Encephalitis (72%)
    - Meningitis (16%)
    - Other neurologic (2%)
  - Non-Neuroinvasive (10%)
- Hospitalized (90%)
- Death (11%, most > 50 years)



Krow-Lucas ER. Vect Borne Zoo Dis 2018; 18(6):286-290  
<https://www.cdc.gov/powassan/data-maps/historic-data.html> (accessed 6/22/24)

## Powassan virus Diagnosis & Care

- Antibody testing best sensitivity
  - CT or MRI may be normal; severe cases often with cerebellar changes (70%)
- CSF: IgM POWV
  - Commercial, State Public Health labs & CDC
  - Needs confirmation by plaque-reduction neutralizing test to r/o cross-reactivity with other flaviviruses
- Other:
  - Viral RNA serum, CSF, tissue
  - Performs best early in illness
  - Immunohistochemistry, fixed tissue
- Treatment: supportive care
- Prognosis: mortality ~ 10%, neurologic sequelae 50%

Plantadot A. Inf Dis Clin N Am 2022;36(3):671-688

## Question 4

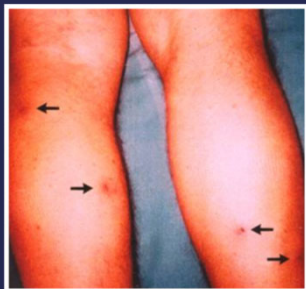
28F presents 8d after from a safari in Tanzania

Fever, mild headache, fatigue x 5d  
Prior to travel, immunized against yellow fever  
Took malaria prophylaxis: atovaquone/proguanil

Temperature is 38.6°, P76, R14, BP 116/70  
Exam is unremarkable except for four punctuate eschars on the legs and bilateral inguinal lymph node enlargement

Lab:  
Thick and thin blood smears (x 2) negative

Four Inoculation Eschars (Arrows)



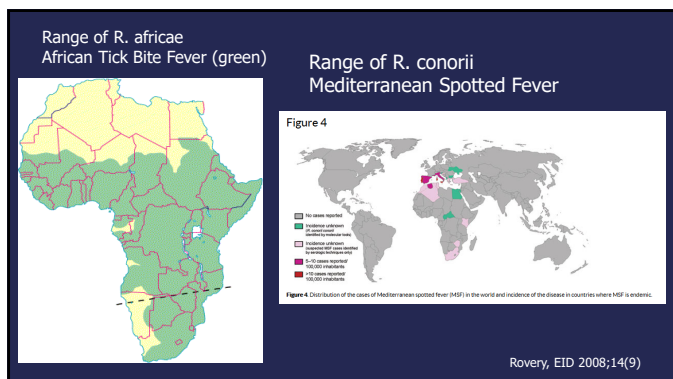
## Question #4 Continued:

Which Of The Following Is The Most Likely Etiologic Agent?

- A. Rickettsia conorii
- B. Rickettsia africae
- C. Rickettsia rickettsii
- D. Anaplasma phagocytophilum
- E. Ehrlichia chaffeensis

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### Clinical Characteristics of *R. africae* Infection

	%
fever $\geq 38.5^\circ$	88
neck muscle myalgia	81
inoculation eschars	95
multiple eschars	54
lymphadenopathy	43
rash (vesicular)	46(45)
death	0

Raoult D, et al. N Engl J Med 2001; 344:1504-10

### African Tick Bite Fever

- Seroprevalence:
  - High in residents, *R. africae*, 30-56%
- Amblyomma ticks (cattle, ungulates)
  - Clusters of cases, multiple eschars
- Incubation period 6-7d
- Dx:
  - Biopsy or swab: PCR or MIFA
  - Serology
- Rx: doxycycline
- Complications unusual

### Rickettsioses and The Returning Traveler Common Cause of Fever After Malaria, Typhoid

Most common: 280 travelers (1996-2008)

- Spotted fever group (83.5%)
  - 87.5% acquired in sub-Saharan Africa
- Others
  - Scrub typhus (5.7%)
  - Q fever (3.6%)
  - Typhus group (2.5%)
  - Human granulocytic ehrlichiosis (0.4%)

Jensenius M, EID 2009;15(11)

### Question #5:

48M presents in October with fever and rash

Supervisor for apartment bldg in Queens, NY. Lives in cellar apt.

Exam: T 39°C  
brown-black 8mm eschar on RLE  
~30 papulovesicular lesions on trunk

8mm inoculation eschar

### Question #5:

Which of the following is the most likely etiologic agent?


- A. *R. rickettsii*
- B. *R. parkeri*
- C. *R. akari*
- D. *R. conorii*
- E. *Borrelia recurrentis*

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## Rickettsialpox

- Organism
  - R. akari
- Reservoir
  - House mouse
- Vector
  - Mouse mites
- Clinical
  - Single eschar
  - Rash: papulovesicular (20-40) or maculopapular
  - Diagnosis
    - PCR swab eschar/vesicle
  - Treatment: doxycycline



Maculopapular rash due to R. akari (CDC)

## Partial DDx of Vesicular Rash


- HSV
- VZV
- Pox viruses
  - mpox
- Rickettsialpox
- African tick bite fever
- Queensland tick typhus

## Scrub Typhus

“Scrub typhus is probably the single most prevalent, under-recognized, neglected, and severe but easily treatable disease in the world”

Paris DH et al. Am J Trop Med Hyg 2013;89:301-7

## Scrub Typhus



- Organism
  - O. tsutsugamushi (> 70 strains)
- Vector
  - Trombiculid mite (chiggers)
- Geography
  - Triangle from Japan to Eastern Australia to Southern Russia (rural)
  - Southern China an endemic focus (Yunnan province)
- Clinical
  - ~1 million cases/yr
  - Severe (~ 35%) high fever
  - Eschar, painful/draining lymph nodes, rash, delirium
    - Meningitis and meningoencephalitis with progressive infection
    - Development of multiorgan system failure
    - Case fatality rates up to 70%



Eschar is often associated with regional lymphadenitis





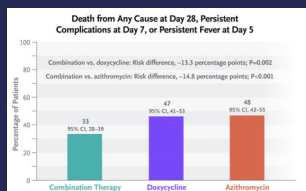
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## Scrub Typhus Treatment

### Treatment

- Doxycycline x 7 days, relapses common
  - Alt: azithromycin (AAC 2014;58:1488-93)
- Combination: appears superior, and safe
  - Doxycycline 200 mg twice daily day 1, then 100 mg twice daily x 6d PLUS Azithromycin 500 mg PO twice daily d1, then 500 mg daily x 6d [Varghese, NEJM 2022]



## Question #6:

31M presents in January with 3d fever, HA, malaise, and myalgia. Works as counselor at wilderness camp in Pennsylvania. Flying squirrels common at camp including residing in the walls of his cabin. Exam is notable only for fever (39.6°; no rash), tachycardia (P110)

A diagnostic test for which of the following is most likely to be positive

- Murine typhus
- Epidemic typhus
- RMSF
- Tularemia
- Relapsing fever

If you read a question with a “flying squirrel”  
You say “epidemic typhus” or  
“*R. prowazekii*”

MMWR 2003; 9 (10); Lancet Infect Dis 2008;8(7):417  
Rare infection in US (1976-2001, 39 cases)  
Generally East Coast  
None with louse exposure (the classic vector) in N America, so not “epidemic” but sporadic  
Most with flying squirrel exposure (*Glaucomys volans*)



Body louse: infestation = pediculosis  
*Pediculus humanus humanus*

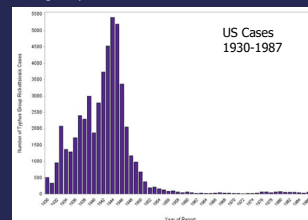
## Typhus: Two Forms

	Epidemic	Endemic
Organism	<i>R. prowazekii</i>	<i>R. typhi</i>
Vector	Louse (body, head)	Flea (rat, cat)
Who	War refugees, crowded conditions/poor hygiene	Worldwide (U.S. Southern California, Texas, Hawaii)
Severity	Lethal	Usually milder, some fatalities
Treatment	Tetracycline Doxycycline Chloramphenicol	Tetracycline Doxycycline Chloramphenicol
Prevention	Boil clothes, delouse (lindane, malathion, permethrin, DDT)	Flea prevention (cats, domestic animals) Reduce rodent population
Recrudescence	Brill-Zinsser Disease (years-decades)	None known

## Murine (or endemic) typhus

- In US, mostly seen in California, Hawaii, and Texas
- Agent: *Rickettsia typhi*
- Infected cat/rat flea feces → skin
- Most don't recall flea bite
- Usually non-specific febrile infection
  - Underdiagnosed
  - ~50% with rash
  - Occasional severe disease:
    - Meningoencephalitis
    - Pneumonitis
    - Shock

Historically, decline w/ better sanitation  
No longer reportable since 1987



Ditrich, Lancet Global Health 2015;3:e104; Blanton Am J Trop Med 2017;96(1):53

CDC, accessed 7/6/2023 <https://www.cdc.gov/typhus/murine/history.html>



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CDC Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives. Protecting People™

Morbidity and Mortality Weekly Report (MMWR)

## Fleaborne Typhus-Associated Deaths — Los Angeles County, California, 2022

Weekly / August 4, 2023 / 72(31):838–843


Incidence: 2010: 1 2022: 171	Deaths 3 (autopsies) -HLH -Myocarditis -Septic shock >late or no doxycycline	Case fatality usually < 1.0% LA Series: 1.8%	Suspect: exposure to rodents, cats Homeless →Doxycycline
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## Murine (or endemic) typhus

- Consider especially febrile illness: CA, TX, Gulf coast
- Dx:
  - Serology *R. typhi* (IFA)
    - Acute/convalescent, 4x rise
    - Cross-reacts with *R. prowazekii* and SFG rickettsia
  - PCR
    - Blood, often negative
- Treatment: No RCTs
  - Doxycycline (preferred)
    - Azithromycin: recent open label trial found azithromycin inferior to doxy
  - Alternatives: limited data
    - Chloramphenicol
    - Levofloxacin
    - Ciprofloxacin

Dittrich, Lancet Global Health 2015;3:e104; Blanton Am J Trop Med 2017;96(1):53  
Newton, CID 2015;68(1 March):739

## Flea-borne typhus (*R. felis*)



- Found globally; underdiagnosed
- Discovered 1990
  - Cat fleas
- Often lumped in with murine typhus
- Usually mild illness but can be severe
  - Fever, headache
  - Rash variable (macular)
  - Eschar in 12%
- Dx:
  - RMSF serology is often reactive
    - Acute/convalescent *R. typhi* serology
  - PCR (tissue)
- Treatment: doxycycline

Martinez MAC, Resp Rep Trop Med 2021;12:1-15

## Other location-specific tick-borne Rickettsioses: partial

- Queensland tick typhus, *R. australis*
  - Australia-Queensland, New South Wales, Tasmania, coastal areas of eastern Victoria
- North Asian tick fever, *R. sibirica*
  - North China; Mongolia; Asiatic areas of Russia
- Tick-borne lymphadenopathy (TIBOLA) or *Dermacentor*-borne necrosis erythema and lymphadenopathy (DEBONEL), ascribed to *R. slovaca* or *R. raoulti*:
  - Europe and Asia.
- Far-Eastern tick-borne rickettsiosis, *R. beilongjiangensis*:
  - Far East Russia and northern China.
- Oriental spotted fever, *R. japonica*:
  - Japan.
- Thai tick typhus, *R. bonoi*:
  - Thailand, Australia, Tasmania, Flinders Island
- Australian spotted fever:
  - *R. marmoris*, Australia.

### Question #7:

- 43F visited southern Missouri on vacation, returns 7d later with fever, headache and diffuse myalgia x 3d
- Physical examination: no findings
- Laboratory evaluation :
  - WBC: 2.1/mm<sup>3</sup> (80% PMNs, 10% lymphocytes, 8% monocytes)
  - Hemoglobin: 7.0 g/dL, hematocrit: 24%
  - Platelets: 105,000/mm<sup>3</sup>
  - AST: 364 U/L, ALT: 289 U/L
  - renal function: normal

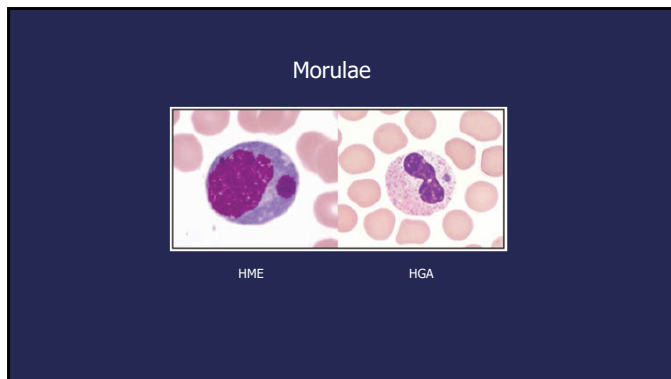
### Question #7

Which of the following is the most likely etiologic agent?

- A. *Anaplasma phagocytophilum*
- B. *Ehrlichia chaffeensis*
- C. *Borrelia hermsii*
- D. *Babesia divergens*
- E. *Borrelia burgdorferi*

# 27 – Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD



## Human Monocytic Ehrlichiosis (HME)

- *E. chaffeensis*
- Vector: Lone star tick
- Rash: ~30%
  - Maculopapular or petechial
- Labs: LFTs ↑, leukopenia, thrombocytopenia
- Mortality 2.7%
- Diagnosis
  - PCR
  - Morulae (2-38%)
  - Serology: acute/convalescent
  - Treatment: doxycycline

Annual incidence (per million population) of reported *Ehrlichia chaffeensis* ehrlichiosis—United States for 2021

0 = 0 to < 0.2   0.2 to < 2.2   2.2 to < 6.4   6.4+   Not Notifiable

Source: CDC <https://www.cdc.gov/ehrlichiosis/data-research/facts-stats/index.html> (accessed 6/22/24)

## Human Granulocytic Anaplasmosis

- *Anaplasma phagocytophilum*
- Vector: *Ixodes scapularis*
- Rash rare
- Labs: LFTs, leukopenia, thrombocytopenia
- Mortality 0.3-0.7% (immunosuppressed ↑ 16 x)
- Diagnosis: same as HME (but morulae seen > 25%)

Annual incidence (per million population) of reported anaplasmosis—United States for 2017

0 = 0 to < 0.13   0.13 to < 1.1   1.1 to < 9.4   9.4+   Not Notifiable

Geography: cross reactivity with HME accounts for most Southern state representation

Source: CDC <https://www.cdc.gov/anaplasmosis/hcp/statistics/index.html> (accessed 6/22/24)

## Other Ehrlichia (less common)

Organism	Vector	Geography	Risk	Mortality
<i>E. ewingii</i> (aka canine Ehrlichia)	Lone star	Most cases in Southcentral US	Immune compromised	Low
<i>E. muris</i>	<i>Ixodes persulcatus</i> <i>H. flava</i>	Europe, Russia, Japan, West Coast US	Older patients	Low
<i>Ehrlichia muris euclairensis</i> (former Ehrlichia muris-like [EML] agent)	Deer tick	Wisconsin, Minnesota	Elderly, immune compromised	Low

### Question #8:

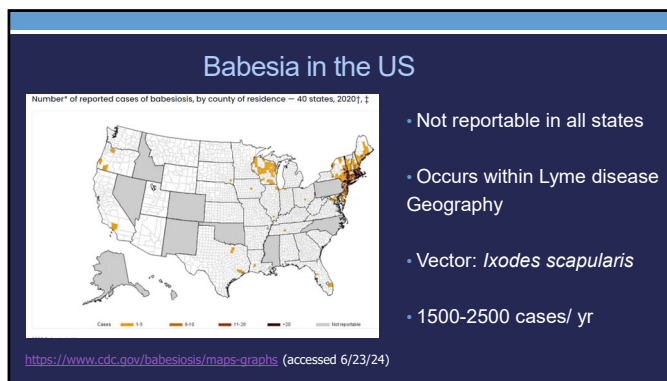
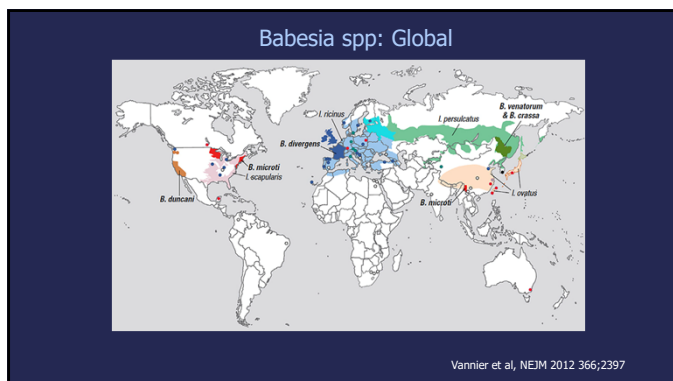
- 48F c/o headache and fatigue worsening over 2 months since May tick bite
  - PMH: negative
  - SH: Married, works from home, has a dog, resides in suburban eastern PA
  - Treated with doxycycline for Lyme disease, no benefit
- Physical examination: afebrile, normal vital signs, no findings
- Laboratory evaluation :
  - WBC: 7.0 cells/mm<sup>3</sup> (70% PMNs, 18% lymphocytes, 12% monocytes)
  - Hemoglobin: 11.8 g/dL, hematocrit: 35%
  - Platelets: 145,000/mm<sup>3</sup>
  - ALT: 22 U/L
  - Babesia IgG 1:128 (positive ≥ 1:64)
  - Blood smear: no parasites

### Question #8:

- The best recommended next step:
  - Check *Babesia duncani* serology
  - Check *Babesia* PCR
  - Repeat blood smear
  - Azithromycin + atovaquone for 7-10 days
  - None of the above

# 27 – Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD



### Babesia species

- Malaria-like parasite, resides in RBCs
- Geography: *Babesia microti* (most cases in U.S.)
  - Nantucket, Martha's Vineyard, Long Island, Mid-Atlantic/New England, upper Midwest (similar to Lyme disease)
- Range of illness: Asx to "flu-like" to fatal

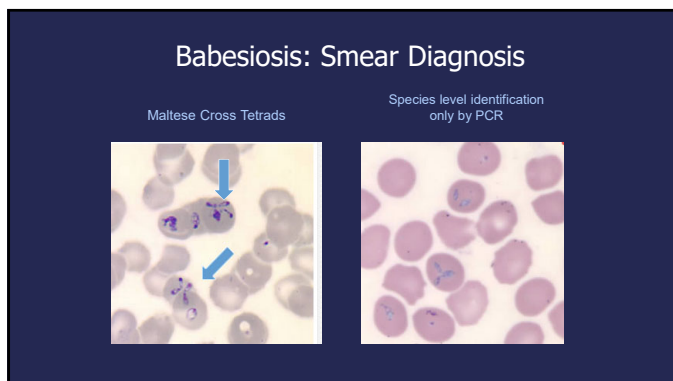
**Was a** common cause of blood transfusion-related infection in US

- Though decreasing through screening
- But question may still appear on the boards

### Severe Babesiosis

- n=34, Long Island NY
- Clinical manifestations
  - 41% Multi-organ failure
    - ARDS, DIC, CHF, ARF
- Risk factors:
  - age >60
  - splenectomy,
  - immunosuppression (e.g., HIV, rituximab)
- Labs
  - increased LTFs,
  - thrombocytopenia
  - anemia (Hb<10),
  - parasitemia (>10%)
- Immunocompromised mortality
  - > 20%

Hatcher JC, et al. Clin Infect Dis 2001; 32:1117-25



### Diagnosis of Babesiosis

- May observe hemolysis
- Wright-Giemsa stained thin blood smears
  - 1-3µ intraerythrocytic merozoites
  - Parasitemia range: 0-80% (may be confused with malaria)
  - Maltese cross: diagnostic (not seen w/ malaria)
  - Quick, if technical expertise available
- PCR: now widely available
  - Highly specific, but often send-out test = delay
- Serology (IFA)
  - High titer or acute/convalescent c/w active or recent infection
  - Low titer, negative smear: don't treat!

# 27 – Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD

## Treatment of Babesiosis

- **Severe (2020 IDSA guidelines)**
  - Atovaquone 750 mg PO q12h + Azithromycin 500 mg IV q24h
    - Previous: quinine + clindamycin (now an alternative)
  - Duration: 7-10d (may require longer for persistent parasitemia or immunosuppressed)
- **Blood exchange transfusion: severe only**
  - B. divergens, many require
  - B. microti, some cases
  - Limited evidence for benefit
    - Severe hemolytic anemia or multi-organ failure
- **Mild-moderate severity**
  - Azithromycin PO plus atovaquone PO

Krause, et al CID 2021; 72 (2) e49-65

## Tickborne Relapsing Fever US

**Borrelia spp. (mainly B. hermsii)**

- Ornithodoros soft ticks (brief, painless)

### Epidemiology

- Western states; 14-45 cases/yr
- Rustic housing and rodents
- Elevation 1500-8000 feet

### Clinical Manifestations

- Fever (relapsing), HA, myalgia, NIV
- Can be severe : ARDS

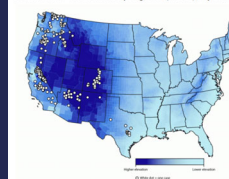
### Laboratory

- AKI, ↓ platelets,
- Dx: blood microscopic exam, PCR

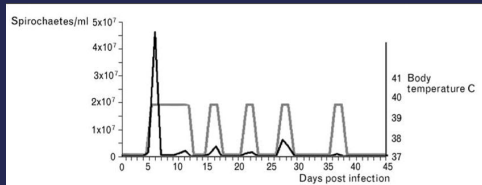
### Rx: PCN, doxycycline

- Jarisch Herxheimer reaction in 54%

FIGURE. Cases\* of soft tick relapsing fever (n = 210), by county† of exposure – United States, 2012–2021

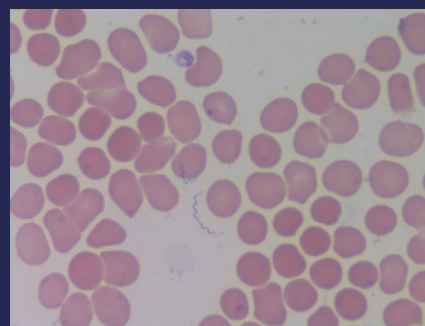


Beeson AM MMWR 2023;72(23):777-781



Relapsing Fever: recurrent bacteremia (black line) correlates with sudden fever (grey).

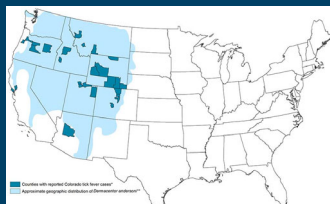
After initial bacteremia, relapses are lower and fever duration somewhat shorter.



Diagnosis: observation of spirochetes in blood film

## Colorado Tick Fever

- Transmission *D. andersoni*
  - 4,000-10,000 feet
- Agent: Coltivirus
- Sx range from
  - Mild febrile flu-like illness
    - May include rash: maculopapular or petechial
  - Rare: severe illness multi-system, neuroinvasive disease
- Labs:
  - ↓ WBC, atypical lymphocytes
  - ↓ plt
- Dx: samples to state lab, some commercial lab testing
  - Not a reportable illness



**Diagnostic Testing**  
 Preliminary diagnosis of Colorado tick fever (CTF) is based on signs and symptoms, dates and sites of travel, activities, and history of potential tick exposure. Rapid and definitive diagnosis is made by reverse transcription-polymerase chain reaction (RT-PCR) to detect the virus in ethylenediamine tetraacetic acid (EDTA) and serum samples.

Timing of specimen collection	Specimens	Preliminary test
1-6 days after symptom onset	Severe (CTF if suspected CNS involvement)	RT-PCR for viral RNA
1-14 days after symptom onset	Severe (CTF if suspected CNS involvement)	Antibody "titering" (antibody RT-PCR for Western Blotting (WB))

## Louse-borne Relapsing Fever (LBRF)

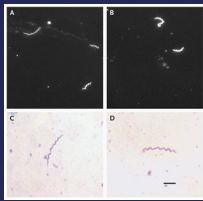
- Organism: *Borrelia recurrentis*
- Vector: Human body louse
- Geography: Worldwide, but now seen in Sudan, Ethiopia, Somalia, Bolivia... (Refugee camps, famine, natural disasters)
- Clinical Illness: More severe than TBRF, (incl. jaundice)
- Therapy: Doxycycline

# 27 – Ticks, Mites, Lice and The Diseases They Transmit

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### Newer Borrelia species: B. miyamotoi

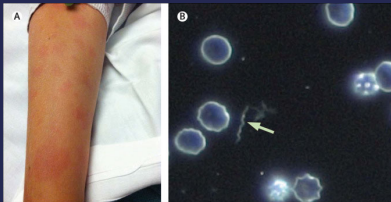
- Unusual vector: Ixodes ticks (larvae?)
- Epidemiology = Lyme disease
- **Appears similar to HGA**
  - Meningoencephalitis in immunocompromised
  - ↓ wbc, ↓ plt, ↑ LFTs
- Diagnosis: blood smear (observing spirochetes), PCR, serology
- Treatment: similar to Lyme disease



Spirochetes in CSF

Telford, Clin Microbiol Infect 2015  
Gugliotta, NEJM 2013

### Borrelia mayonii



5 of 6: acute febrile illness with rash (macular)  
1 of 6: 1 months knee pain/swelling  
To date: only see in in Minnesota and Wisconsin

Pritt et al. Lancet ID 2016;16(5):556

### Cluster of Tick Paralysis Cases

- Four cases within 20 miles of each other
  - Ages 6, 58, 78, 86 years
- Ticks on neck or back
  - Usually dog ticks or Rocky Mt wood ticks
- Ascending motor paralysis without sensory loss
- Treatment: remove tick = cure
- Pathogenesis: neurotoxin in tick saliva

MMWR 2006; 55: 933-5

### Question #9:

A 59 y.o. man from Missouri presents with fever (39°), headache, myalgia, anorexia, nausea, one week after removing an engorged tick from his groin. No travel.

Exam: unremarkable except ill appearing, no rash.  
Lab: wbc 2300 plt 42,000 ALT 111

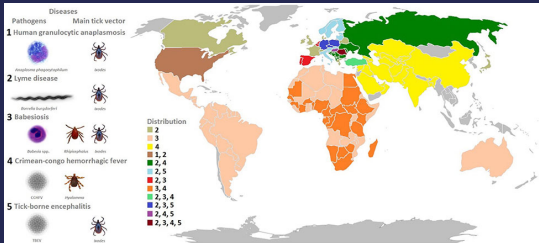
Suspect ehrlichiosis (but no morulae on blood smear)

### Question #9:

After sending appropriate diagnostic tests the patient has not improved after three days of doxycycline. Which of the following is the most likely etiologic agent?

- R. rickettsii
- B. burgdorferi
- R. parkeri
- Heartland virus
- Severe fever with thrombocytopenia syndrome virus

### But wait: There's More (#4) and More (#5)



Disease	Main tick vector	Distribution
1 Human granulocytic anaplasmosis	G22	1, 2, 3, 4
2 Lyme disease	Ixodes	1, 2, 3, 4
3 Babesiosis	Ixodes	1, 2, 3, 4
4 Crimean-congo hemorrhagic fever	Hyalomma	2, 3, 4, 5
5 Tick-borne encephalitis	Ixodes	2, 3, 4, 5

Front Cell Infect Microbiol, 2017;7:114

# 27 - Ticks, Mites, Lice and The Diseases They Transmit

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## Tick-borne infections: some testable points

- Rash: RMSF rash appears after several days of fever and viral-like prodrome
  - Meningococcal rash is earlier
  - No bite site (tache noire)
  - Give doxycycline, even for kids
- Blood smear maybe helpful
  - Morulae: PMN = Anaplasma, Monocyte = Ehrlichia
  - Spirochete: relapsing fever Borrelia or B. miyamotoi
  - Erythrocyte inclusions: Babesia

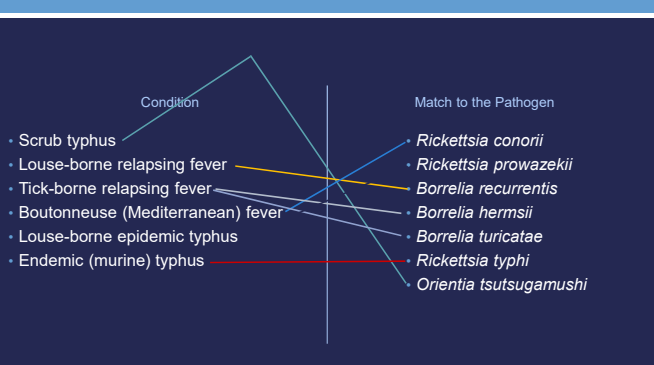
## Tick-borne infections: some testable points?

- Babesia:
  - Cause of blood transfusion infection in US
  - Splenectomy or immunocompromise = risk severe infection risk
- Co-infections in the US: may complicate some infections especially after black-legged tick (*I. scapularis*) bite
  - Lyme disease + Babesia OR Lyme disease + HGA mostly
- Flying squirrels: epidemic typhus
- Rodent infested urban house: Rickettsialpox
  - Mouse mites.
  - Tache noire first → > dozen papules/vesicles

Key features of select tick, louse, and mite-borne diseases

Disease	Usual Organism	Geography	Eschar	Rash	High fever	Comment
<b>TICK-BORNE</b>						
RMSF	<i>R. rickettsii</i>	N.C.S. America	No	Yes	Yes	Serious
STARI	Unknown	S, SC, MA	No	Yes (EM)	No	Mild
<i>R. parkeri</i>	<i>R. parkeri</i>	Gulf, South, Atlantic	Yes (2)	Yes	No	
African tick bite fever	<i>R. africae</i>	Sub-Saharan Africa	Yes (2)	Yes	No	Mild
HME	<i>E. chaffeensis</i>	S, SC, MA	No	Yes (+/-)	Yes	Cytopenias Transaminitis
HGA	<i>A. phagocytophylum</i>	NE, NY, MA, MW	No	Yes (+/-)	Yes	Cytopenias Transaminitis
Babesiosis	<i>B. microti</i>	NE, NY, MA, MW	No	Yes (+/-)	Yes	Spirochetes in blood smear
TBRF	<i>B. hermslii</i>	W Mountains	No	No	Yes	
<b>LOUSE-BORNE</b>						
Epidemic typhus	<i>R. prowazekii</i>	Worldwide	No	Yes	Yes	War, refugee camps serious
<b>MITE-BORNE</b>						
Rickettsialpox	<i>R. akari</i>	Worldwide	Yes (1)	Yes (V)	No	Mouse exposure
Scrub typhus	<i>O. tsutsugamushi</i>	India, Asia, N. Australia	Yes	Yes	Yes	Serious

C	Central	NY	New York
EM	Erythema Migrans	RMSF	Rocky Mountain Spotted Fever
HGA	Human Granulocytic Anaplasmosis	S	South
HME	Human Monocytic Ehrlichiosis	SC	South Central
MA	Middle Atlantic	SE	Southeast
MW	Mid West	STAR1	Southern Tick Associated Rash Illness
N	North	TBRF	Tick-borne Relapsing Fever
NE	New England	V	Vesicular
		W	West



Thank You!  
and  
The End.



*B. mayonii*  
Spirochete in Culture

Pitt, Clin Micro and Inf 2022

0:21 / 0:21

Speed: 1x

End of Track